Multicomponent Approach to the Synthesis, Characterization and Biological Evaluation of Substituted Pyran Derivatives

SYNOPSIS

SUBMITTED TO

Faculty of Sciences

UNIVERSITY DEPARTMENT OF CHEMISTRY

B. N. MANDAL UNIVERSITY, MADHEPURA

FOR THE DEGREE OF

DOCTOR OF PHILOSPHY

BY

Name: Ramanand Kumar

PAT-2022

Class Roll No.: 06

Exam Roll No.: CHE-05/22

Email: kumarramanand106@gmail.com

B.N.MANDAL UNIVERSITY, LALOO NAGAR, MADHEPURA

SYNOPSIS OF RESEARCH WORK FOR Ph.D. DEGREE IN THE FACULTY OF SCIENCE (CHEMISTRY)

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(i) Work Plan

a. Purpose and need of the study

Multicomponent reactions (MCRs) have emerged as powerful synthetic tools that allow three or more reactants to combine in a single operation, affording structurally complex products with excellent atom economy and operational simplicity. These reactions are widely used in drug discovery because they enable rapid access to diverse molecular frameworks with high efficiency and minimal waste.

The present study focuses on the design, synthesis, and biological evaluation of substituted pyran derivatives. Pyran-based heterocycles constitute an important class of biologically active molecules exhibiting antimicrobial, antiviral, anticancer, antiproliferative, antitumor, CNS-active, and agrochemical properties. Due to this broad biological profile, the development of new pyran derivatives remains an active research area. In addition, 4H-pyrans, tetrahydrobenzo[b]pyrans, and related fused systems have shown potential in treating disorders such as schizophrenia, Alzheimer's disease, and other neurodegenerative conditions.

Advances in catalytic systems, such as metal salts, magnetic nanoparticles, ionic liquids, and heterogeneous catalysts, have facilitated efficient access to these compounds under mild and sustainable reaction conditions. The present work aims to explore MCR-based methodologies for developing novel substituted pyran derivatives and to evaluate their biological potential.

Review of Literature of proposed work

Pyran derivatives and their fused analogues have long been recognized as valuable heterocycles due to their broad biological and pharmacological significance. Literature reports highlight that 4H-pyrans and tetrahydrobenzo[b]pyrans exhibit antimicrobial, antiviral, anticancer, anticoagulant, antioxidant, and anti-inflammatory properties. Several derivatives also display CNS activity and are being explored for the treatment of neurological disorders. Recent research emphasizes the use of multicomponent reactions for the rapid synthesis of functionalized pyrans under environmentally benign conditions. A variety of catalysts, including $CeCl_3 \cdot 7H_2O$, Fe_3O_4-based nanocomposites, ionic liquids, and silica-supported bases, have been effectively used to improve yields and reaction rates. Moreover, alternative energy sources such as microwave irradiation and electrochemical methods have enhanced synthetic efficiency. Pyranopyrazoles, chromenes, and pyrimidine-fused pyrans have also gained attention due to their diverse pharmacological applications. Overall, the literature strongly supports the continued development of new pyran derivatives for potential therapeutic use.

b. Details of the project with chapterization

Chapter- I: Introduction

Chapter- II: Survey of previous works

Chapter- III: Experimental

Chapter- IV: Result and Discussion

Chapter- V: Conclusion

Chapter I: Introduction

This chapter will provide an overview of heterocyclic chemistry with emphasis on pyran derivatives, their structural features, and biological importance. The scope, relevance, and need for multicomponent strategies in synthesizing pyran-based molecules will be discussed.

Chapter II: Survey of Previous Works

A detailed review of existing literature, including synthetic methodologies, catalytic systems, and reported biological activities of pyrans and fused heterocycles, will be outlined. Gaps in previous research and justification for the proposed study will be highlighted.

Chapter III: Experimental

This chapter will describe the reagents, instruments, reaction procedures, and optimized conditions used for multicomponent synthesis. Purification techniques and characterization methods (NMR, FT-IR, MS, etc.) will also be presented.

Chapter IV: Results and Discussion

Structural characterization, reaction optimization, mechanistic insights, and biological activity results will be analyzed. Comparisons with literature and interpretation of structure–activity relationships will be included.

Chapter V: Conclusion

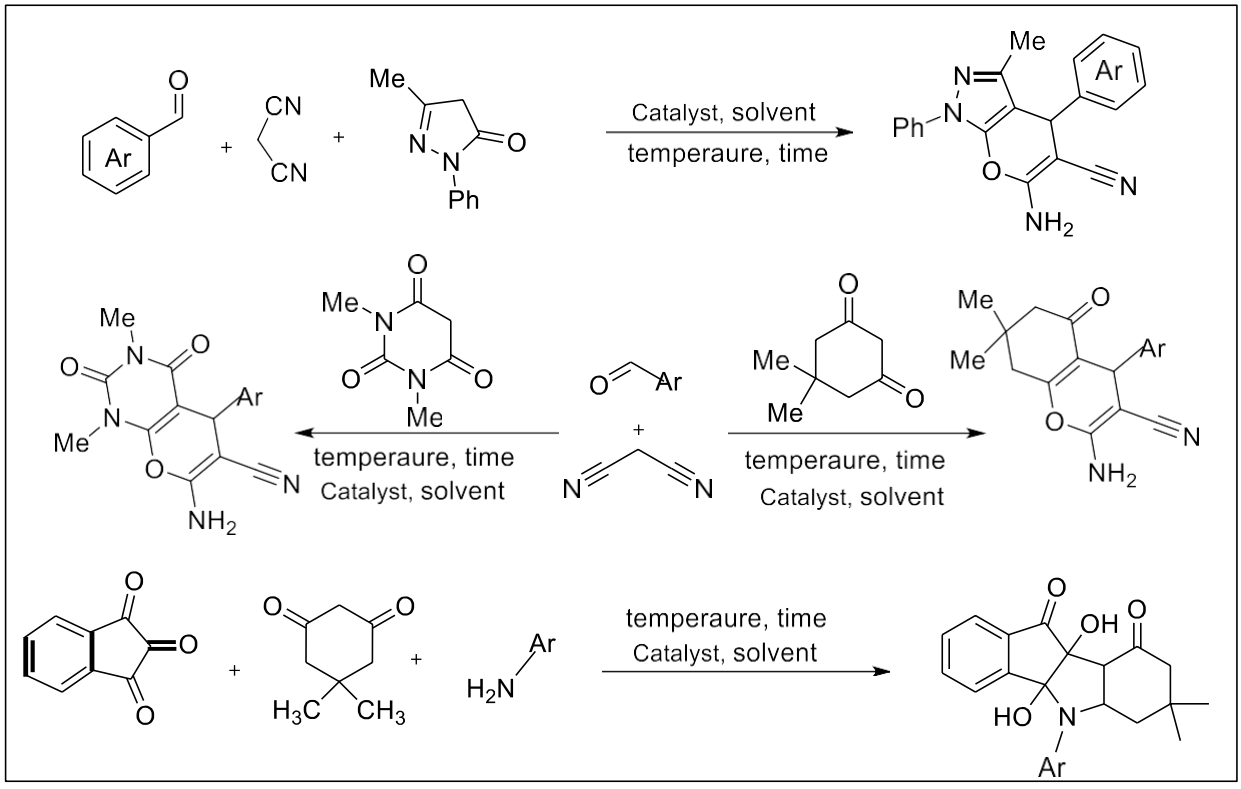
This chapter will summarize the major findings, highlight the significance of the developed synthetic protocols, and propose future research directions.

c. Hypothesis

It is hypothesized that multicomponent reactions can provide an efficient, eco-friendly, and high-yielding route to structurally diverse pyran derivatives. These compounds, owing to their heterocyclic frameworks, are expected to exhibit significant biological activity, potentially outperforming or complementing known analogues. Optimized catalytic systems are anticipated to enhance reaction efficiency, selectivity, and product diversity.

d. Methodology

The proposed methodology involves applying optimized multicomponent reaction conditions to synthesize a diverse range of pyran-based heterocycles. Initially, pyranopyrazole derivatives will be prepared through a one-pot reaction of aromatic aldehydes, malononitrile, and pyrazolone under mild catalytic conditions to afford the desired products efficiently. This strategy will then be extended to the synthesis of pyrimidine-fused tetrahydropyran and tetrahydro-4H-chromene derivatives using aldehydes, malononitrile, and 1,3-dimethylbarbituric acid, enabling the construction of highly functionalized fused heterocyclic systems under similar reaction conditions. To further demonstrate the versatility of the developed protocol, multi-fused indeno-indoledione derivatives containing four stereocenters will be synthesized via the reaction of ninhydrin with various aromatic or aliphatic amines and dimedone, forming single-diastereomer products (Scheme-1)



Scheme 1: Synthesis of Pyran Derivatives.

e. Bibliography

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Name of Research Scholar:- Ramanand Kumar

Class Roll No. :- 0 6

Examination Roll No. :- CHE-05/22
Session :- 2025-2028

Mobile No. :- 8809311248

Email id :- k u m a r r a m a n a n d 1 0 6 @ g m a i l . c o m

Signature of Research Scholar